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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/783,635	02/20/2004	Ann Marie Schmidt	56613-A JPW/AJM/AAB	1285

7590 02/23/2007

John P. White
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, NY 10036

EXAMINER	
EMCH, GREGORY S	
ART UNIT	PAPER NUMBER
1649	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/783,635	SCHMIDT ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,32,49,51 and 58-75* is/are pending in the application.

4a) Of the above claim(s) *1* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32,49, 51 and 58-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/18/04 & 5/2/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicants' elections with traverse of Group II, claims 32, 49 and 51, and the species of quinine in the reply filed 26 December 2006 are acknowledged. The traversal is on the ground(s) that examining Groups I and II together would not be a search burden on the Examiner because a search of the prior art relevant to the claims of Group II would provide the relevant art for Group I. Applicants assert that Groups I and II relate to methods all pertaining to the inhibition of a peptide to RAGE.

Applicants' attention is directed to MPEP 808.02 which states that "Where the related inventions as claimed are shown to be distinct under the criteria of MPEP 806.05 (c-i), the examiner, in order to establish reasons for insisting upon restriction, must show by appropriate explanation one of the following: (A) Separate classification thereof; (B) A separate status in the art when they are classifiable together; (C) A different field of search." Thus, Applicants' traversal is not found persuasive because although the methods generally relate to methods of inhibiting a peptide's interaction with RAGE, the methods recite structurally and functionally distinct elements that are not required one for the other. More specifically, Group II requires inhibiting the interaction of AGE with RAGE in a subject, wherein Group I does not recite this limitation. Also, in Group II there is no requirement of a test compound(s) (as in Group I), which encompasses a plurality of potential molecules. Similarly, Group II requires administering quinine to a subject, whereas Group I does not require an administration

step. Thus, as set forth in the restriction requirement of 22 August 2006, these distinct methods are often separately characterized and published in the art and would add undue search burden if examined together (p.3).

Furthermore, as set forth in the Restriction requirement, Group I is classified in class 435, subclass 7.2, whereas Group II is classified in class 424, subclass 130.1. The separate classification established for each Group also demonstrates that each distinct Group has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search. Thus, the Restriction requirement is still deemed proper and is therefore made FINAL.

The election of species requirement is hereby withdrawn on the grounds that the species are sufficiently few enough that examining them together would not be a serious search burden.

Claim 1 is hereby withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim.

Response to Amendment

Claims 58-75 have been added as requested in the amendment filed on 26 December 2006. Following the amendment, claims 1, 32, 49, 51 and 58-75 are pending in the instant application.

Claims 32, 49, 51 and 58-75 are under examination in the instant office action.

Information Disclosure Statement

Signed and initialed copies of the IDS papers filed 18 October 2004 and 02 May 2005 are enclosed in this action.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 32 and 58-73 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 7,101,838.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

In the instant case, although the conflicting claims are not identical, they are not patentably distinct from each other because claim 1 of the '838 Patent is drawn to a method of inhibiting atherosclerosis in a subject suffering from hyperlipidemia, which comprises administering to the subject a polypeptide comprising an extracellular domain of sRAGE, said polypeptide capable of inhibiting an interaction between amyloid-β peptide (an AGE) and RAGE in an amount effective to inhibit atherosclerosis in a subject.

The instantly claimed method is an obvious variation of the claims as set forth in the '838 patent because, an agent capable of inhibiting the interaction of AGE with RAGE is defined by the instant specification as a polypeptide comprising at least a portion of sRAGE (p.16, lines 26 and 27). Furthermore, claims 2 and 3 of the '838 patent recite treating mammals and humans, as in the instant claim 58. Also, claim 8 of

the '838 patent recites the same limitations as the instant claim 59. In addition, claim 4 of the '838 patent recites the same limitation as the instant claim 63 and claim 6 of the '838 patent recites the same limitation as the instant claim 65. Claim 9 of the '838 patent recites administering the polypeptide with a pharmaceutically acceptable carrier as in the instant claims 69-73. Therefore, the claims of the '838 patent are obvious over claims 32 and 58-73 of the instant Application.

Claims 32 and 58-73 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 56-62 of copending Application No. 09/498,459.

Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 56 of the '459 Application is drawn to a method for treating a subject afflicted with atherosclerosis, which comprises administering to the subject an agent capable of inhibiting the interaction between amyloid-β peptide with RAGE.

The instantly claimed method is an obvious variation of the claims as set forth in the '459 application because as disclosed in the instant specification, subjects of the instantly claimed method include those with atherosclerosis (p.15, line 29) as in the '459 application. Also, claims 57 and 58 of the '459 application recite treating mammals and humans, as in the instant claim 58. Further, claim 61 of the '459 application recites the same limitations as the instant claim 59. Additionally, claim 62 of the '459 application recites administering the polypeptide with a pharmaceutically acceptable carrier as in

the instant claims 69-73. Therefore, the claims of the '459 application are obvious over claims 32 and 58-73 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32, 49, 51 and 58-75 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claims are to directed to a method for inhibiting the interaction of an advanced glycation endproduct (AGE) with a receptor for advanced glycation endproduct (RAGE) in a subject, which comprises administering to the subject an amount of a compound effective to inhibit the interaction between the AGE and RAGE in the subject.

The claims are genus claims because the specification (and claims) do not set forth the structure of the multitude of molecular species, i.e., the claimed "compound"

including derivatives of quinine or quinidine (including those with a different chemical structure but the same overall charge as quinine or quinidine) that are encompassed by the claims. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In the instant case, there is no identification of any particular portion of any particular structure that must be conserved to practice the claimed invention. Accordingly, in the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Further, although the claims recite a functional limitation, i.e., inhibiting the interaction between AGE and RAGE, with the exception of quinine or quinidine (as disclosed on p.39), the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed molecules. Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of

isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only methods reciting quinine or quinidine, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicants are reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 32, 49, 51 and 58-75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of inhibiting the interaction between AGE and RAGE in diabetes mellitus and in inflammation, for example, with quinine or quinidine, and thus, treating said disease states, does not reasonably provide enablement for inhibiting the interaction between AGE and RAGE and thus, treating any disease state, with any compound including any derivative of quinine or quinidine (including those with a different chemical structure but the same overall charge as quinine or quinidine). The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

The claims require the use of a broad genus of potential molecules, and as stated above, Applicants have not described all of the common features of the genus such that the skilled artisan could identify individual members. As broadly claimed, the methods of the invention can comprise use of any number of molecules, e.g., nucleic acids, polypeptides including antibodies, small molecules or peptidomimetics. If one considers only a subset of the molecules encompassed by the claimed methods, e.g., polypeptides, the potential amino acid sequences encompassed by the claims have particular structures, the predictability of which is complex and outside the realm of routine experimentation. Since detailed information regarding the structural requirements of the multitude of potential amino acid sequences encompassed by the claims are lacking, and given the lack of working examples reciting any and all of the sequences encompassed by the claims, it is unpredictable as to which variations, if any, meet the limitations of the claims. Furthermore, Applicants have not limited the activity of the target polypeptides encompassed by the claims, thus contributing to the

unpredictability of the claimed methods. Therefore, making the compounds and testing them for the claimed "biological activity" would constitute undue experimentation.

Accordingly, it is well known in the art that even two polypeptides differing in structure by only one amino acid residue can have completely different functions. For example, Mickle et al. (Med Clin North Am. 2000 May; 84(3): 597-607) teaches that cystic fibrosis (CF) is an autosomal recessive disorder caused by abnormal function of a chloride channel, referred to as the cystic fibrosis transmembrane conductance regulator (CTFR) (p.597). In this polypeptide channel, a mutation of a single glycine to aspartic acid at position 551, gives rise to the CF phenotype. Also, a single phenylalanine deletion at position 508 gives rise to the CF phenotype, thus showing that even the substitution or deletion of a single amino acid in the entire 1480 amino acid CFTR protein sequence can have dramatic and unpredictable effects on the function of the protein.

Additionally, it is known in the art that even a single amino acid change in a protein's sequence can drastically affect the structure of the protein and thus the architecture of an entire cell. For example, Voet et al. (Biochemistry. 1990. John Wiley & Sons, Inc. 126-129 and 228-234) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pp.126-128, section 6-3A and page 230, column 2, first paragraph). Also, Yan et al. (Science 290: 523-527,

2000) teaches that in certain cases, a change of two-amino acid residues in a protein results in switching the binding of the protein from one receptor to another. Thus, as outlined above, the predictability of the structure/function of the amino acid sequences as claimed is complex and outside the realm of routine experimentation.

Moreover, the claims encompass methods of treating any disorder characterized by the interaction between AGE and RAGE. However, Applicants do not disclose any actual or prophetic examples on expected performance of specific agents used in specific disease states. As such, the art recognizes the unpredictability of treating lupus, for example. As such, Bird et al. (Pathology. 1995 Apr;27(2):136-9) teach that quinine and quinidine usage has a causal association with lupus associated pathology (entire document, e.g., abstract). Further, Rosa-Re et al. (Ann Rheum Dis. 1996 Aug;55(8):559-60) teach that quinine induces a lupus-like condition (entire document). Thus, quinine and quinidine administration would not be desirable in all of the claimed disease states.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. Due to the large quantity of experimentation necessary to practice the claimed invention, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the claimed methods, and the breadth of the claims which encompass variant molecules, undue experimentation would be required of the skilled artisan to practice the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 32, 58, 59, 62, 63 and 66-73 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/26913 to Stern et al. (cited in IDS dated 18 October 2004).

The claims are to directed to a method for inhibiting the interaction of an advanced glycation endproduct (AGE) with a receptor for advanced glycation endproduct (RAGE) in a subject, which comprises administering to the subject an amount of a compound effective to inhibit the interaction between the AGE and RAGE in the subject.

The '913 document teaches a method for treating a subject with a condition associated with interaction of an amyloid-β peptide (an AGE) with a receptor for advanced glycation endproduct (RAGE), which comprises administering to the subject an agent capable of inhibiting the interaction between amyloid β-peptide and RAGE, the agent being present in an amount effective to inhibit the interaction between the amyloid β-peptide and RAGE, thereby treating the subject (p.12, lines 19-27), thus meeting the limitations of claim 32. Further, the reference teaches that the subject may be a mammal or a human (p. 12, lines 33-34), thus meeting the limitations of claim 58. The '913 document also teaches that the administration may be intralesional, intraperitoneal,

intramuscular, intravenous, infusion, liposome-mediated delivery, topical, nasal, oral, ocular or otic delivery (p.12, line 34 – p.13, line 1), thus meeting the limitations of claim 59. The '913 document also teaches that the subjects may have a number of disorders, e.g. a condition associated with amyloid β-peptide fibril or with aggregation of amyloid β-peptide including conditions associated with aging such as Alzheimer's disease and senility, diabetes, renal failure, hyperlipidemic atherosclerosis, ALS, MS and Down's syndrome, most of which are conditions characterized by patients with inflammation (p.12, lines 29-33; p.13, lines 5-6; p.16, line14), thus meeting the limitations of claims 62, 63 and 66-68. The reference teaches pharmaceutically acceptable carriers, including diluents, an aerosol, an phosphate buffered saline and various other suitable intravenous carriers, oral carriers including those with flavor additives, a topical carrier microencapsules, encapsulation in polymers and in erythrocyte ghosts and time release implants (p.14, lines 6-12; pp.16-18), thus meeting the limitations of claims 69-73.

Since the document teaches all the elements of the claims, claims 32 and 58, 59, 62, 63 and 66-73 are anticipated by WO 97/26913 to Stern et al.

Claims 32, 49, 51, 60, 63, 68-70 and 72 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/09046 to Daines.

The claims are to directed to a method for inhibiting the interaction of an advanced glycation endproduct (AGE) with a receptor for advanced glycation endproduct (RAGE) in a subject, which comprises administering to the subject an

amount of quinine or quinidine or a derivative thereof effective to inhibit the interaction between the AGE and RAGE in the subject.

The '046 document teaches methods for treating a subject for various conditions, including but not limited to chronic inflammation, arthritis and diabetes mellitus, comprising administering quinine or quinidine or pharmaceutically active salts thereof in an amount effective to treat the condition (p.3, lines 23-30; p.6, lines 18-26). Although the reference does not appreciate inhibiting the interaction between AGE and RAGE, this would nonetheless be an inherent outcome of administering quinine and quinidine in a subject with the conditions referred to above. It is noted that neither the instant claims nor the instant specification teach the specific amounts of quinine or quinidine effective to inhibit the interaction between AGE and RAGE, which would distinguish the claimed method from that taught by the prior art. Thus, treating diabetes mellitus, for example (a disease characterized by the interaction between AGE and RAGE), with quinine or quinidine or derivatives thereof would inhibit said interaction, as in the prior art. Thus, the reference meets the limitations of claims 32, 49, 51, 63 and 68.

The '046 document also teaches treatment of mammals and humans (p.3, line 30), thus meeting the limitations of claim 58. Further, the '046 document teaches daily administration (p.9, line 27), thus meeting the limitations of claim 60. The reference teaches pharmaceutically acceptable carriers, including diluents, administered with the active compounds of the invention (p.6, lines 18-26), thus meeting the limitations of claims 69 and 70. The reference also teaches formulations with oral, intravenous,

aerosol and topical carriers (p.6, line 27 – p.9, line 20), thus meeting the limitations of claim 72.

Since the document teaches the elements of the claims (both expressly and inherently), claims 49 and 51 are anticipated by WO 97/09046 to Daines.

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 32, 61-63, 66, 67 and 69-73 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,864,018 to Morser et al (cited in IDS dated 18 October 2004).

The '018 patent discloses a method for inhibiting atherosclerotic plaque formation in a diabetic subject, which comprises administering to said subject compositions capable of inhibiting an interaction between AGE and RAGE. Such compositions may be used to reduce the pathological effects of various diseases (col.4, lines 10-34, 54-64; col.5, lines 4-38; col.6, lines 1-16; col.19, lines 9-15), thus meeting the limitations of claim 32. The '018 patent discloses administration of the polypeptides to human and mammalian patients (col.18, lines 64-67; col.19, lines 1-31), thus meeting the limitations of claim 58. Further, the patent discloses administration may be oral, intravenous, intraperitoneal, intramuscular, topical or liposome mediated (col.19, line 57 – col.20, line

7), thus meeting the limitations of claim 59. The patent teaches dosage of the compounds of from about 0.0001 10 mg/kg body weight to about 10 mg/kg body weight (col.19, lines 50 and 51), thus meeting the limitations of claim 61. Also, The '018 patent discloses prevention or treatment of disorders, such as Diabetes Mellitus, diabetic macrovasculopathy (atherosclerosis), neuropathy, nephropathy, age-related disorders, amyloidosis including Alzheimer's disease (col.19, lines 6-24), thus meeting the limitations of claims 62, 63, 66 and 67. The patent teaches pharmaceutically acceptable carriers, such as water and saline (diluents), liposomes and sustained release devices (col.19, line 57 – col.20, line 32), thus meeting the limitations of claims 69-73.

Since the patent discloses all the elements of the claims, claims 32, 61-63, 66, 67 and 69-73 are anticipated by U.S. Patent No. 5,864,018 to Morser et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 32, 58-63 and 66-73 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/26913 to Stern et al. (cited in IDS dated 18 October 2004).

The claims are to directed to a method for inhibiting the interaction of an advanced glycation endproduct (AGE) with a receptor for advanced glycation endproduct (RAGE) in a subject, which comprises administering to the subject an amount of a compound effective to inhibit the interaction between the AGE and RAGE in the subject.

The '913 document teaches a method for treating a subject with a condition associated with interaction of an amyloid-β peptide (an AGE) with a receptor for

advanced glycation endproduct (RAGE), which comprises administering to the subject an agent capable of inhibiting the interaction between amyloid β-peptide and RAGE, the agent being present in an amount effective to inhibit the interaction between the amyloid β-peptide and RAGE, thereby treating the subject (p.12, lines 19-27), as in claim 32. Further, the reference teaches that the subject may be a mammal or a human (p. 12, lines 33-34), as in claim 58. The '913 document also teaches that the administration may be intralesional, intraperitoneal, intramuscular, intravenous, infusion, liposome-mediated delivery, topical, nasal, oral, ocular or otic delivery (p.12, line 34 – p.13, line 1), as in claim 59. The '913 document also teaches that the subjects may have a number of disorders, e.g. a condition associated with amyloid β-peptide fibril or with aggregation of amyloid β-peptide including conditions associated with aging such as Alzheimer's disease and senility, diabetes, renal failure, hyperlipidemic atherosclerosis, ALS, MS and Down's syndrome, most of which are conditions characterized by patients with inflammation (p.12, lines 29-33; p.13, lines 5-6; p.16, line14), as in claims 62, 63 and 66-68. The reference teaches pharmaceutically acceptable carriers, including diluents, an aerosol, an phosphate buffered saline and various other suitable intravenous carriers, oral carriers including those with flavor additives, a topical carrier microencapsules, encapsulation in polymers and in erythrocyte ghosts and time release implants (p.14, lines 6-12; pp.16-18), as in claims 69-73.

The '913 document does not teach the timing of administration, as recited by claim 60, or the amount administered, as recited by claim 61.

However, in the instant case, these factors are clearly result effective parameters that a person of ordinary skill in the art would routinely optimize (see MPEP 2144.05). Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal dosages and administration protocols. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization would have been obvious at the time of Applicants' invention.

Accordingly, claims 32, 58-63 and 66-73 are unpatentable over WO 97/26913 to Stern et al.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached on Monday through Friday from 9AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached at (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gregory S. Emch, Ph.D.
Patent Examiner
Art Unit 1649
01 February 2007

ELIZABETH KEMMERER
PRIMARY EXAMINER